OnePot

Full Automated Batch Reactor



One Reactor from Complex Synthesis to Biotech



OnePot in Brief



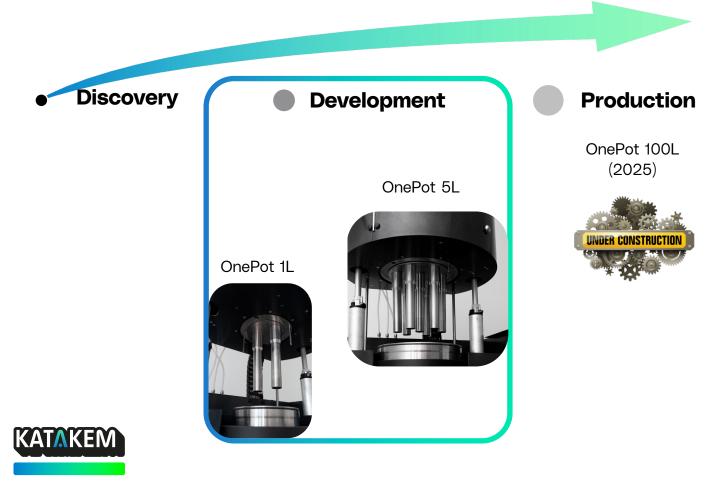
OnePot is a fully automated batch reactor. What does it mean? That OnePot can execute all the operations needed to perform a chemical reaction:

- Dosing and inlet the reagents, liquids, gases and solids.
- Heating and Mixing through the Innovative Matrix in Batch Technology
- Extract product or "clean" waste

Simultaneously, OnePot acquires all the parameters needed to follow the reaction:

- Temperature
- pH (0-14)
- Pressure
- Weight

OnePot application in the Chemical Chain



Application Fields



Multi-step Synthesis processes

Fermentation and Cells cultures

High value of API and Raw materials

High control on process parameter

High QC restrictions

GMP/GLP Regulatory

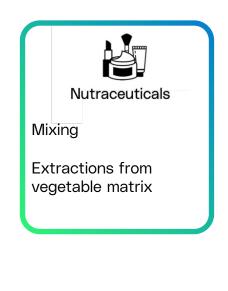


Emulsions, gelification

Extractions from vegetable matrix

High viscosity bulk

Fermentation and Cells cultures



Main Pains in Development

In the last 100 years, labs have not changed much. During a chemical process's development phases, a chemist needs to use **multiple no-connected instruments**. Unfortunately, the low level of automation during the operational phase forces the operator to perform **many tasks manually**.

Each year, this **manual, low-tech approach** causes the waste of millions of manhours and **makes companies lose billions of €.** *These lost are connected to:*

> Low Reproducibility of a chemical process

Slow knowledge Sherability

- Baker, M. 1,500 scientists lift the lid on reproducibility. Nature 533, 452– 454 (2016). <u>https://doi.org/10.1038/533452a</u>
- ATCC, Six factors affecting reproducibility in life science research and how to handle them. NaturePortfolio <u>https://www.nature.com/articles/d42473-</u> 019-00004-y





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The consequences

Every year, Europe loses a staggering 4 B€ in the wasted time of its most highly skilled personnel and the disposal of valuable chemical reagents.

New products may take up to **2 years** to be released in the market due to a delay in production.

Missed Revenues

Missed Investments

Lost of competitive advantage

SUSTAINABILITY

ECONOMY

Usage of chemical reagents which can not be reused and then must be wasted

Highly specialized personnel are undervalued, leading to frustration.

The potential risk of accidents is significantly amplified by frequent repetition of manual operations

Millions of people are deprived of the opportunity to improve their quality of life.

OnePot Value Proposition

Time reduction	Cost reduction
 It allows knowledge storage and reduce the waste of time in case of employee turnover. 	 Reduce the need of specialized operators
 File sharing is possible in one click and saves months of work. 	 Reduce the wasted reagents in the development phase
 Enhance the time invested by chemists in high value activities, reducing the time for 	Recover materials to re-use or sell
new discovery	 Reduce energy consumption by 90% than traditional reactors.
Ready for Companies	ESG-Driven
 In case of unpredicted demand, production can be increased in minutes by using a new OnePot. Automated Warehouse Management. GMP-ready Fast scale-up from R&D to Production (Future development of OnePot 100L) 	 Eliminate the risk of explosions, toxic fumes, and material spillage. Eliminate emissions by working in a closed-loop, sealed environment Enable Circular Economy



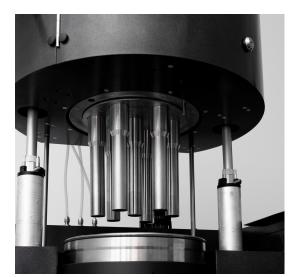
OnePot is the solution!

By *Automating* all the operations needed to perform a chemical transformation we can achieve:

>95% REPRODUCIBILITY

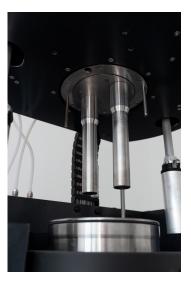
Thanks to automation, for the first time in history, we can *Fully-Digitalize* a chemical process to have:

Instant SHAREABILITY



OnePot 5L

OnePot 1L

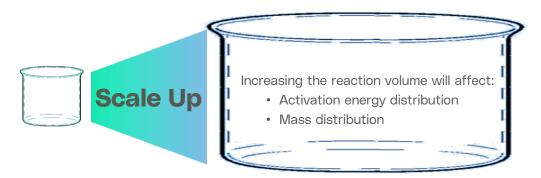


- Controlled and sealed reaction volume
- Dosing reagents: liquid, solid and gases
- Working volumes on a scale between 200mL to 5L
- Pressure control
- Temperature control with the Matrix in batch Technology
- Vortex free mixing
- Sampling outlet to make analytics in line
- pH measurements
- Wight control
- Extraction of Product and Waste
- Multi-reactor interconnection for circular-economy or multi-step processing



The Matrix in Batch Technology

It is NOT a Problem of Chemistry



The Matrix in Batch Technology is an innovative way to **control the energy distribution** (i.e. heating) directly from the inner of a batch process. Technologically, it is possible by the **Spot**. It is equipped with several Cells that can be controlled individually to read and set the temperature. This kind of control can be used to **scale up a chemical process reducing the efforts**. Moreover, all the energy is transferred to the bulk with 100% efficiency. The possibility of manipulating the energy distribution can open the way to explore innovative chemistry space.

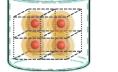
The Concept

Ideally discretize the volume in ordered sub-volume cells

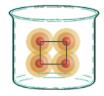
Set a heater and a sensor for each cell. It will define an ordered matrix





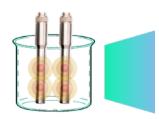


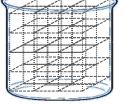


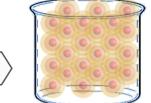


The Spot as Enabling Technology

Direct Scale Up by linearly scale the cells Matrix in the Batch volume to **reproduce the activation energy distribution**











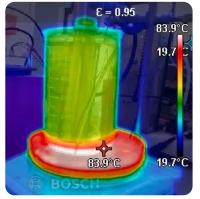
M. Francardi, M.Oliverio – Patent registrated in Italy n. IT202000008245A1 – Property of B4Chem SRL

A. Caravella, et. Al. Optimization of temperature distribution in the novel powerto-heat matrix-in-batch OnePot© reactor, Front. Energy Res. 10, (2022) <u>https://doi.org/10.3389/fenrg.2022.964511</u> Spots can rotate to have a high-performance mixing and reach high mass uniformity



Spot at work

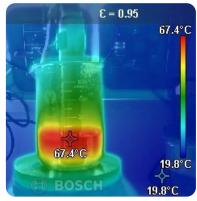
Classic Hot-Plate Heating



Vs

19.7°C Active Volume of a Single Cell: 250÷300 ml

Single Cell Spot Heating



Independent control of each Cells in the Matrix















How to work with OnePot

The OnePot control system is designed with a revolutionary principle that aims to **capitalize on know-how**. By storing all the operations performed with OnePot and retaining the operator's information, we can ensure that every user is equipped with the knowledge they need to succeed. The first step in using OnePot is to log in as a user. And with an "Administrator" account, you can add an unlimited number of users, making OnePot the perfect tool for any team.

KATAKEM	
Email	
Password	
Forgot Password?	
Log In	

All the machines installed in a workspace operate under the coordination of a single central server, known as HubServer. A single server can manage up to 50 OnePots. OnePot allows you to work both remotely and locally.

There are two operating modes available for OnePot:

- Local operations: An operator can work directly in front of OnePot with the 13" touch display mounted. In this mode, OnePot can perform a single stage, and then the operator can design the next one and run it until the procedure is completed. This method is used during the development phase of a new reaction that still needs to be developed. Each stage will be performed automatically by OnePot.
- **Remote operations**: In this mode, we can have OnePot perform an entire procedure, which is an ordered sequence of stages. Procedures can also be designed to be performed directly in an automated manner. Through this mode, we can study the effects of even small variations in individual parameters on the process results, enabling the possibility of carrying out a DOE (Design Of Experiment)

Remote Control
Local Control

(Full Procedure Run)
(Data Storage)

(Data Storage)

Hub Server

(Data Storage)

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How to Design a Procedure

Dashboard	ID	Name 🗸	Version	Creator ψ	Last run 🗸	Onepot				
OnePot Procedures	1	Procedure Name	1.2.3	1111122	10 am 01/02/22	OnePot Lab 1	۲	C	£	⊚
Processes Reports	2	Procedure Name	1.2.3	1111122	10 am 01/02/22	OnePot Lab 1	۲	C	£	⊚
Warehouse Users V	3	Procedure Name	1.2.3	11111122	10 am 01/02/22	OnePot Lab 1	۲	C	£	⊚
은 User List 온* Add users	4	Procedure Name	1.2.3	11111122	10 am 01/02/22	OnePot Lab 1	۲	C	£	୲୲
	5	Procedure Name	1.2.3	11111122	10 am 01/02/22	OnePot Lab 1	۲	C	£	⊚
				1 2 3	4 5 →					
Settings										
Documentation										

 Both remote and local, you can visualize all the procedures stored in the HubServer. It is not dependent on which OnePot the Procedure was run. All the work produced by the lab is always disposable.

- **RUN** a procedure you have already designed.
- **Edit** a receipt with the safety to never override your work: OnePot will generate a new version each time you modify it.
- **Import** a procedure from another workspace/Lab.

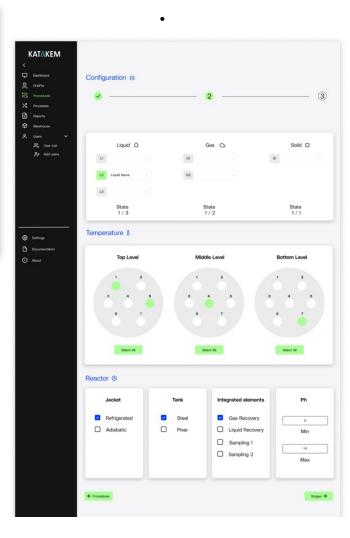
• Create a new procedure.

(Manual design is possible only working locally)

	edures 😄
Deshboard	
E OnePot	
Procedures	Name Version
X Processes	Procedure Name 1.1.0
Reports	Description
Ø Warehouse	Briefly describe the procedure.
A Users ✓	second astrocate cost fordations of
R User List	
Add users	Compatible OnePot
	OnePot Model 5L v 1.2.3 V
	Select Type
	O
	$ \rightarrow $
Settings	Manual Automatic
Documentation	
About	
	Configuration

Before to start the OnePot Configuration must be set:

- Define which reagents are connected to which inlet.
- Define from which Cells of the Matrix in Batch you want visualize the data during the run. Anyway, all data will be acquired.
- Select if you use the adiabatic or the cooled chamber
- Select if you will work with the steel or glass vessel
- · Select which outlet will be used
- Select the pH range

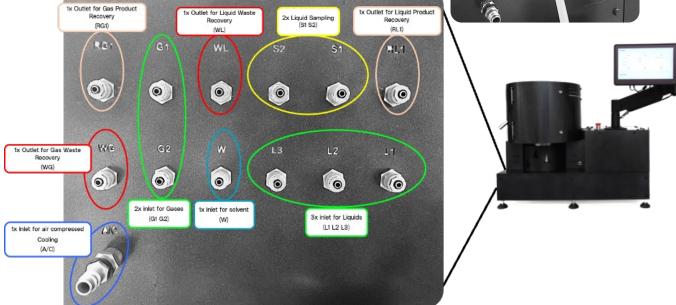




Reagents Configuration

On the left side of OnePot is present a panel for the connection of the inlet and outlet both for **liquids** and **gasses**. The connections are very easy and need the usage of a PTFE pipe (4mm internal diameter and 6mm external diameter)





Instead, a single slot for **solid** is present on the top. It must already be in the form of powder with a grain size under 2mm. The standard slot can be loaded up to 100mL of powder. But, if you need more, it can be extended up to 1L with an accessor.



All the reagents not needed to be pre dosed. OnePot will pick alone the right amount as it is designed in the Procedure



Warehouse Management

To choose a reagent for an inlet, it is necessary for the reagent to be available in the **Warehouse**. Each output from a Procedure (also known as Product) will be added to the warehouse and can be used as a reagent for subsequent reactions. For liquids, OnePot can determine the correct reagent by its density. Before initiating an automated Procedure, OnePot will verify whether there is enough material available to carry out the Procedure. The management of raw materials can be linked to the administrative software to establish a connection with the supply chain that is **compliant with Industry 4.0 standards**.

۸	Wareho	use 🖒			Q			AD	D		•••••	:	
	Id	Name	Formula ↑	Cas Number	State ↑	Density ↑	Quantity ↑						
9	38	essential oil mix			liquid		100	C	Û				
₽. X.	37	Ethanol	СНЗСН2ОН	64-17-5	liquid	0.794	1500	C	Û				
	36	Glycerol	СЗН8ОЗ	56-81-5	liquid	1.26	860	C	Û				
	35	Acritamer 941		78651-20-8	solid	0.3	10	C	Û				
	19	Water	H2O	7732-18-5	liquid	1	1254	C	Û				
				1								•	
			٨		Acido lattico	乙							
			>	1	Name *					Molecular Fo	rmula		
			P	(Acido lattico					С3н603			
			9 17	:	State *					CAS Number			
			×	(Liquid				×	v 79-33-4			
			₿ \$		Quantity *					Density			
			ĉ	(200					1.2			
												ADD	2

Select the right jacket for Vessel

Refrigerated





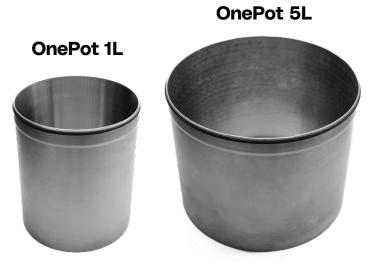


To cool down the temperature, the system uses a compressed air jacket. To ensure proper operation even at **-20°C**, an inlet pressure (A/C inlet in the left side panel) of 7 bar at 850 NL/min is required. The bindings are user-friendly due to the implementation of standard fast bindings.



The Vessel

OnePot comes with a standard vessel that is made of **316L** stainless steel However. it doesn't allow you to see the process's evolution from the inside. If you want a Pyrex model, you can request it. With this model, you will only be able to see inside if you use the adiabatic jacket, which has special slits. But using this version requires more attention from the operator to ensure safe handling of the reagents and products generated.



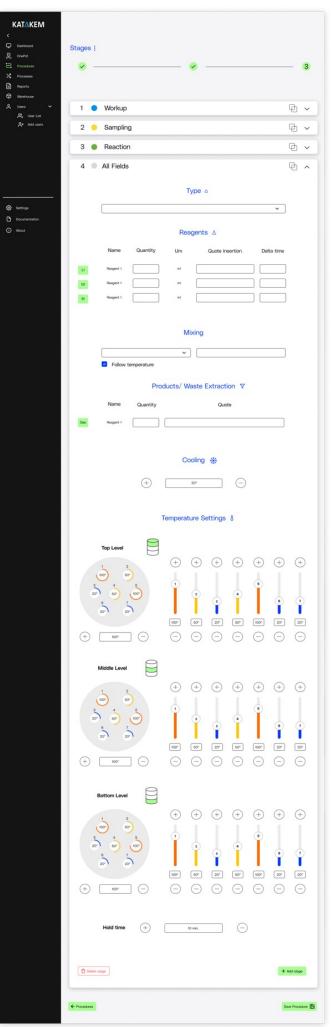
pH and construction materials

OnePot comes equipped with a pH meter that is fixed and parallel to the vertical axis, with a stem length to cover the entire extension of the vessel. This allows for continuous monitoring of the pH throughout the reaction. **The pH meter can work in a range of 0-14**.

All reagents and products in OnePot come into contact only with **PTFE**, the material of which all the tubes and coverings of the pumps and valves are made, and **316L stainless steel**, the material of which the Vessel, the Spot casings, the vessel closure interface, the entire OnePot body (which is Teflon-coated), and all the fluidic fittings are made of. This allows OnePot to **work safely with extreme reagents or products, both strongly acidic and basic**.

It should be noted that these limits are modified if you decide to operate with a Pyrex Vessel.





The Stage

A Procedure consists of one or more Stages, each defining a single block of operations. A Stage allows you to design all the operations you need to perform simultaneously. There is no duration limit for a single stage.

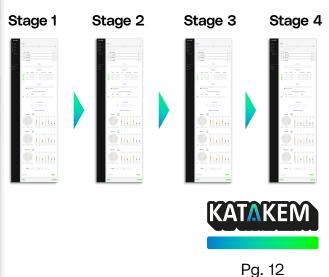
For example, if you need to insert 200mL of water, heat it to a set temperature for 1 hour, and mix it at 100RPM, you can do it all in a single Stage. Alternatively, you can split these operations into several Stages for better organization.

Each Stage can be identified as Workup, Sampling, or Reaction, but this only serves as a visual aid to simplify the Procedure design for the operator.

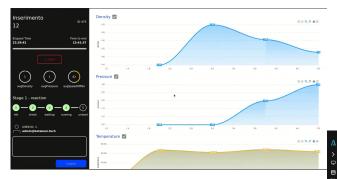
However, there are some limitations to be aware of. Only one liquid reagent can be inserted in a Stage, and it's not possible to both inlet and outlet a liquid in the same Stage. For each Stage, it's possible to set a temperature for each cell of the Matrix in Batch.

If you're working locally, each Stage must be run before designing the next one.

A Procedure can be composed of an infinite number of Stages.



RUN and Reports

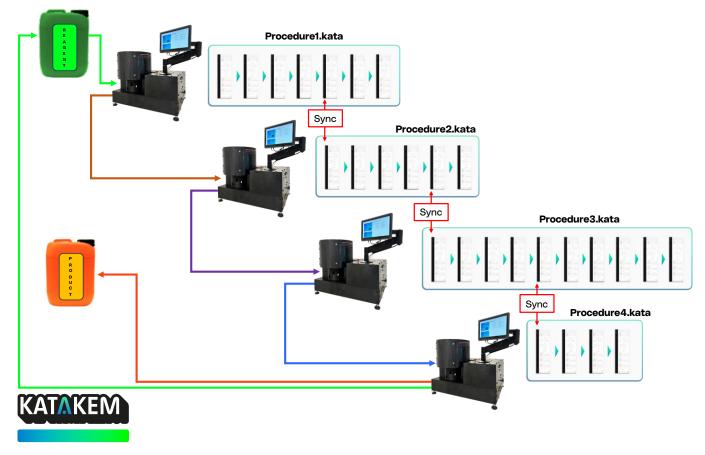


Once the Procedure is terminated, a full Report is saved in the specific section. From local, these Reports can just be viewed, while from remote you can download them. In reports are present all the parameters, independently from what we observe during the Run and for each of them is possible to download the .CSV file. During the Run, operators can monitor various parameters locally and remotely. They can modify the parameters under monitoring during the Run.

Id	ID Procedure	Runned By ↓	Onepot	Date ↓	
196	189	20	15	2023-03-15	۲
197	189	20	15	2023-03-15	۲
198	189	20	15	2023-03-15	۲
199	189	20	15	2023-03-15	۲
200	189	20	15	2023-03-15	٢
201	189	20	15	2023-03-15	٢
202	189	20	15	2023-03-15	٢
203	189	20	15	2023-03-15	۲

The Process

A Process involves coordinating multiple OnePots in sequence using a multi-procedural approach. Stage discretization is used for synchronization to begin specific procedures. The product from the n-procedure becomes a reagent for the (n+1) and so on. In that way is possible to perform **complex multi-step processes**. More, clean waste can be recovered to use as secondary raw material to put again in the loop, in a **Circular Economy** approach. A Process can be exported as a file as well for the Procedure.



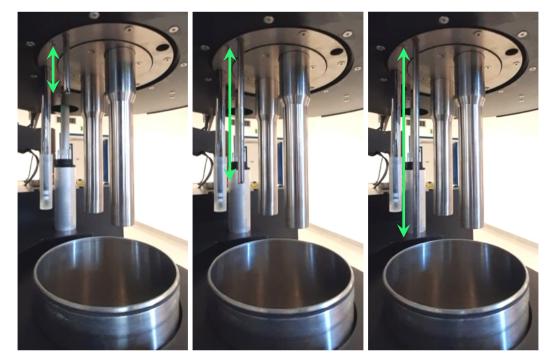
Some more operative details

The OnePot design concept eliminates the need for operator-environment interaction within the reaction volume. This can only be achieved by providing chemists with the necessary flexibility to develop new procedures. To this end, we have incorporated unique features.

The Extrusors to control the inlet/outlet quote

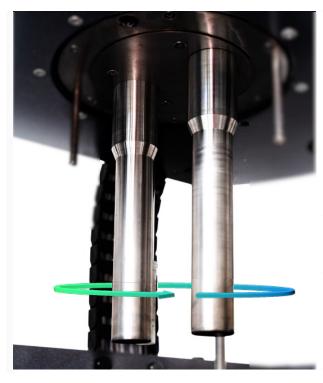
Inlet and Outlet for liquids pass through the same line. Each time the tubes are cleaned by the solvent connected in the W inlet from the panel, preventing contaminations and reactions inside the pipes. In design the stage is possible to define a quote at which inlet the reagent ore outlet the product or waste. For gasses is possible to define a quote only for inlet, to generate bubbling effects. Here is reported the function that, as a function of the insert volume, can indicate to the operator which quote inlet or outlet.

OnePot 1L	Δ Quote of 1mm = Δ Volume of 20mL
OnePot 5L	$\Delta Quote of 1mm = \Delta Volume of 50mL$





The Mixing



As mentioned earlier, the rotation of the responsible Spots is for the mixina This mechanism process. ensures uniformity in mass and energy throughout the entire volume of the vessel, even at low rotation speeds. In contrast. а standard steerer or anchor would require a rotation speed of 6000 RPM to achieve the same level of uniformity that OnePot can ensure at 150RPM. The cylindrical shape and distribution of the Spots in the vessel volume make the mixing quality possible. The low rotation speed is also necessary to prevent vortex formation, which can cause variability. When scaling up a procedure or process for production purposes, the mixing process requires no more effort than a conventional approach. This depends on the scope of the mixing, which aims to achieve higher uniformity in a shorter time.

Sampling lines for in line analytics

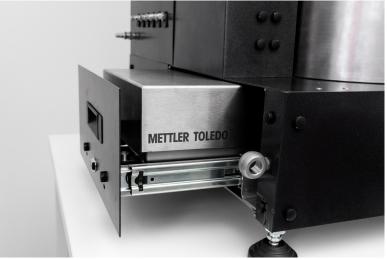
Two sampling lines can be utilized to extract a small amount of the solution. This is why it is possible to set a "Sampling" stage. During the development phase, when working locally, these lines can be used to monitor the reaction's evolution before defining the next stages. When running the procedure remotely, these lines can be used for in-line quality control.

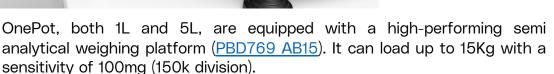
Self-Diagnostic

We continuously monitor all the equipment that is electro-actuated, such as motors, pumps, valves, and guides, to ensure that they are functioning properly. This helps us prevent any unexpected downtime for maintenance. In case of any issues, it becomes easier to identify the problem and focus on solving it, which saves both time and money.



Top quality equipment for Top performances

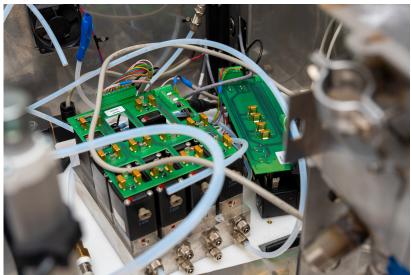




As pH-meter, the standard equipment is <u>INPRO 4800I/SG/225</u>. The InPro 4800i offers stable and precise measurement under extreme process conditions due to its highly alkaline resistant pH glass membrane, double chamber gel electrolyte reference system, and chemical resistance.

burkert Fluid Control Systems

As a partner in developing the manifolds for liquids and gasses control, we collaborate with Burkert for a customized solution. This collaboration gives us the possibility to introduce customizations for specific applications.

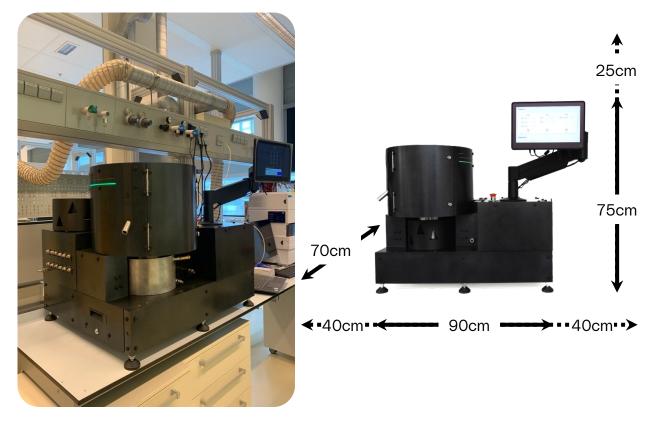


METTLER

TOLEDO



Information on Installation



Aspiration characteristics

Required OnePot should be placed inside a laminar flow fume hood if the dimensions, including head handling, permit. Otherwise, the solution of an aspirated arm with a hat between 50cm and 75cm can be adopted. The system must be sized to ensure a suction flow rate between 250 and 500 m3/h; the diameter of the pipe must be consistent with the suction adopted. Preferably, the vacuum arm should be equipped with replaceable EPA filters.

IT requirements

A server (HubServer) comes with OnePot. Installing only one server for each OnePot network and not for a single reactor is necessary. The server supplied is a tower but can be installed inside a rack if needed. The LAN used to install the system must be private IPv4 -VLAN not supported.

A static IP for the HubServer as well as a static IP for each OnePot, must be provided. The following ports are used and must therefore be enabled:

- 80 web interface
- 443 https web interface
- 1883 endpoint for OnePot connection



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Applications Fields

PROCESSES

- ANHYDRIFICATION
- DECANTATION*
- DISTILLATION
- FRACTIONAL DISTILLATION
- EXTRACTION*
- ✓ FILTRATION*
- LIQUID-LIQUID SEPARATION
- ORGANIC SYNTHESIS
- V WORK-UP

X CHROMATOGRAPHY X HIGH-VACUUM DISTILLATION X RECRYSTALLIZATION X SPECTROSCOPIC TECHNIQUES

REACTIONS	
✓ ACID-BASE	✓ SYNTHESIS OF GAS PRODUCTS
✓ BIOLOGICAL	ELECTROPHILIC AROMATIC SUBSTITUTION
V CLICK CHEMISTRY	VNUCLEOPHILIC SUBSTITUTION
CONDENSATION	
✓ HYDROLYSIS & SAPONIFICATION	
✓ MCR	
✓ ORGANOMETALS	
✓ OXIDATION	
V PERICYCLIC	X HYDROTERMIC DEGRADATION
V POLIMERIZATION	X PETROLEUM SYNTHESIS
✓ RADICAL	X HIGH PRESSURE
✓ REDUCTION	



Specifications

Quantity	UM	Minimum value	Average value	Maximum Value
Width (1L=5L)	cm		90	
Depth (1L=5L)	cm		70	
Height 1L (5L)	cm	74 (79)		96,5 (101,5)
Total weight	Kg		120	
Power Supply	V		220 AC	
Working Temperature	°C	-20		200
Working Pressures	barr	0,2		5
Working pH range	рН	0		14
Mixing	RPM	0		150
Liquid inlet	n.		3	
Gas inlet	n.		2	
Liquid Sampling outlet	n.		2	
Requested compressed air for cooling	barr		7	
Solids Insert Slot	n.		1	
Solids Insertion Volume	dm ³	0,0002		1 (5)
Gas Inlet Pressure	barr	> P Vessel		10
Spot_2C (1L)	n.		2	
Spot_3C (5L)	n.		7	
Working Volume (OP-5L)	ml	450		5500
Working Volume (OP-1L)	ml	200		1200
Power Consumption (1L)	Kw/h	0,1	0,7	1,35
Power Consumption (5L)	Kw/h	0,1	1,2	2,6



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